

December 6, 2002

James R. Cooper  
Executive Director  
SOCMA Urea Resins Group  
1850 M Street, NW  
Suite 700  
Washington, DC 20036

Dear Mr. Cooper:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for methylated 4,5-dihydroxy-1,3-bis(hydroxymethyl)-2-imidazolidinone, posted on the ChemRTK HPV Challenge Program Web site on February 26, 2002. I commend the SOCMA Urea Resins Group for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Urea Resins Group advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at [tsca-hotline@epa.gov](mailto:tsca-hotline@epa.gov).

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director

Risk Assessment Division

Enclosure

cc: C. Auer  
A. Abramson  
W. Penberthy  
M. E. Weber

**EPA COMMENTS ON CHEMICAL RTK HPV CHALLENGE SUBMISSION:  
METHYLATED 4,5-DIHYDROXY-1,3-BIS(HYDROXYMETHYL)-2-IMIDAZOLIDINONE**

**SUMMARY OF EPA COMMENTS**

The sponsor, the SOCMA Urea Resins Group, submitted a test plan and robust summaries to EPA for methylated 4,5-dihydroxy-1,3-bis(hydroxymethyl)-2-imidazolidinone (CAS No. 68411-81-4) and for the analogs, 4,5-dihydroxy-1,3-bis(hydroxymethyl)-2-imidazolidinone (CAS No. 1854-26-8) and 4,5-dihydroxy-1,3-bis(methoxymethyl)-2-imidazolidinone (CAS No. 3001-61-4), dated December 3, 2001. EPA posted the submission on the Chemical RTK HPV Challenge Web site on February 26, 2002.

EPA has reviewed the submission and has reached the following conclusions:

1. Physicochemical and Environmental Fate. EPA agrees with the submitter that testing is not necessary for the water solubility and the partition coefficient endpoints. The information for boiling point, melting point, and vapor pressure provided by the submitter is inadequate and thus testing may be needed for these endpoints. EPA agrees with the submitter that testing is not necessary for photodegradation, stability in water, and fugacity. The data provided for biodegradation are inadequate. The submitter needs to provide measured biodegradation data for this substance.
2. Health Effects. Adequate data are available for all health endpoints on the analog. EPA considers these data adequate to address all endpoints for the purposes of the HPV Challenge Program.
3. Ecotoxicity. The toxicity endpoints for fish and aquatic invertebrates have been adequately addressed for the purposes of the HPV challenge program. However, the algae endpoint is inadequately addressed and therefore testing is necessary.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

## COMMENTS ON THE METHYLATED 4,5-DIHYDROXY-1,3-BIS(HYDROXYMETHYL)-2-IMIDAZOLIDINONE CHALLENGE SUBMISSION

### General

The submitter provided little information about the substance other than that it is methylated to an unknown extent and is handled commercially as an aqueous solution. This makes it difficult for a reviewer to determine data adequacy, especially in the areas of physicochemical properties and fate. For example, some values were obtained on a substance that was 13% water. It would be helpful to know whether this represents a typical initial product or is the result of adding water to an initially anhydrous substance. Furthermore, while the sponsored substance is clearly a mixture, the lack of information on the degree of methylation, average molecular weight, *cis* to *trans* ratios, etc. hinders a satisfactory evaluation.

### Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility)

Adequate data are available for partition coefficient and water solubility.

*Melting point, boiling point, and vapor pressure.* The values provided were obtained with a test substance containing 13% water. Testing of an aqueous concentrate will not give appropriate values even if conducted in accordance with OECD guidelines. The submitter needs to provide measured data for the anhydrous substance or explain why this is not feasible.

Environmental Fate (photodegradation, stability in water, biodegradation, and transport and distribution fugacity)

Adequate data are available for photodegradation, stability in water, and fugacity.

*Biodegradation.* The submitter did not provide biodegradation data for the sponsored substance. Data from several biodegradation studies of the analogous parent compound 4,5-dihydroxy-1,3-bis(hydroxymethyl)-2-imidazolidinone were provided. However, methylation of the parent compound may yield a material of significantly different biodegradability, suggesting that the HPV substance itself needs to be tested. Moreover, one of the analog studies concluded that elimination of the test substance was "probably not due to biodegradation." Therefore, the submitter needs to provide measured biodegradation data on CAS No. 68411-81-4, following OECD Guideline 301.

*Fugacity.* Any new measured physicochemical property or environmental fate data should be used as inputs to the models.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate data are available for all endpoints for the purposes of the HPV Challenge program.

EPA agrees with the submitter's proposal to use data on the parent compound/analog, 4,5-dihydroxy-1,3-bis(hydroxymethyl)-2-imidazolidinone, to address all endpoints, given the similar chemical structures and toxicity profiles as discussed in the test plan. The submitter needs to address deficiencies in the robust summaries.

*Acute Toxicity.* Although the four studies submitted were not adequate individually, they address the endpoint adequately by the weight of the evidence and the consistent LD<sub>50</sub> values.

*Reproductive Toxicity.* This endpoint is addressed by documentation of the evaluation of reproductive organs in a 90-day repeated-dose toxicity study and the availability of an adequate developmental toxicity study.

Ecological Effects (fish, invertebrates, and algae).

The endpoints for fish and aquatic invertebrates appear adequately addressed for the purposes of the HPV Challenge Program. However, testing for the green algae endpoint on the sponsored chemical is required owing to the limitations of toxicity predictions by the modeling program and to toxicity concerns raised by the measured algal toxicity of the nonmethylated analog.

**Specific Comments on the Robust Summaries**

Environmental Fate

*Fugacity.* The submitter needs to provide the input values to its model III calculations.

Health Effects

*Acute Toxicity.* The missing information for the acute oral toxicity robust summaries includes: strain, sex, number of animals, study design, period of post-treatment observation, incidence of mortality, analytical and statistical method, and a range or 95% confidence interval for the LD<sub>50</sub>.

*Repeated-Dose Toxicity.* The submitter needs to provide the following omitted

information: the purity of the test material, the specific hematology, clinical chemistry and urinalysis parameters, and the organs, especially reproductive organs, that were examined for gross and microscopic pathology, which were included in the reproductive toxicity robust summary.

*Genetic Toxicity (in vitro).* For the second Ames test the dose units of mg/plate in part of the assay should be : g/plate. The robust summary also omitted the following information: the number of replicates per concentration and the number of metaphases per concentration that were examined.

*Reproductive Toxicity.* The submitter needs to indicate whether the doses in the rat repeated-dose toxicity study were adjusted for purity of the test chemical. The submitter also needs to add information from the repeated-dose toxicity robust summary about the effects observed (moderate bilateral mineralization of testes) in male rats dosed with 6000 mg/kg/day.

#### Ecological Effects (fish, invertebrates, and algae).

The submitter needs to provide the following information to confirm data adequacy: test concentrations; method for preparing test solutions; age of the organisms at test initiation; control mortality; pH, dissolved oxygen, water hardness, and temperature readings throughout the test; number of replicates per test concentration; and number of organisms per replicate.

#### **Followup Activity**

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.